
Role of intradermal skin tests in the evaluation of clinically relevant respiratory allergy assessed using patient history and nasal challenges

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Background: Skin testing, correlated with patient history, is the accepted method of identifying clinically relevant aeroallergen sensitivity. Traditionally, intradermal tests are believed to be more sensitive in identifying aeroallergen sensitivity than the epicutaneous and percutaneous methods. Therefore, many allergy practitioners use the epicutaneous or percutaneous method first and, if the results are negative, follow up with intradermal tests.

Objectives: To compare the epicutaneous, percutaneous, and intradermal methods to determine their sensitivity to patient history and to evaluate the value of intradermal tests when epicutaneous and percutaneous test results are negative.

Methods: Participants were evaluated for rhinoconjunctivitis symptoms and then were skin tested using the prick and Multi-Test II (MTII) methods. Intradermal tests were performed when prick and MTII test results were negative to an aeroallergen. Participants with negative prick and MTII test results and corresponding positive intradermal test results underwent nasal challenges with evaluation by anterior rhinomanometry.

Results: Compared with patient history, average sensitivity for MTII was 77% and for the prick method was 62%. When MTII results were negative, 17% of intradermal tests corresponded with probable patient histories of allergy but none with positive nasal challenge results. Nasal challenge results were similar to those of the negative control group and significantly different from those of the positive control group ($P < .001$).

Conclusions: The MTII tests are more sensitive and equally specific compared with the prick method. When MTII results are negative, positive intradermal test results are unlikely to identify clinically relevant aeroallergen sensitivity. Routine performance of intradermal tests when MTII results are negative is likely to be of low clinical yield.

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INTRODUCTION

Skin testing for immediate-type sensitivity is the preferred method for identifying respiratory allergies. Traditionally, it has been believed that intradermal skin tests are more sensitive in identifying specific IgE antibody to an aeroallergen than either the epicutaneous or the percutaneous skin test method. As a result, it has been the practice of many physicians to perform epicutaneous or percutaneous skin tests first, and if the results are negative, to follow up with intradermal tests. However, it has been noted since the 1930s that a positive intradermal test result does not always correlate with clinical symptoms. Grow and Herman¹ and Rackemann and Simon² noted that as many as half of the individuals with positive intradermal skin test results did not show a correlat-

ing history. Both groups concluded independently that a positive intradermal test result without correlation to patient history is of little value. More recent studies have now brought into question the value of performing follow-up intradermal tests when epicutaneous or percutaneous skin test results are negative. Nelson,³ Reddy,⁴ Brown,⁵ and Wood⁶ and their colleagues reported that in participants with a negative skin prick test result, a corresponding positive intradermal test result did not identify clinically important respiratory allergy. The investigation by Mènardo et al⁷ determined that the percutaneous Multi-Test actually gave a better correlation with patient history and radioallergosorbent testing than either the prick or the intradermal method. In this study, we first sought to determine the relative value of the epicutaneous (skin prick), percutaneous (Multi-Test II [MTII]; Lincoln Diagnostics, Decatur, IL), and intradermal methods compared with patient history. Because patient recall history can be flawed or confounded by sensitivity to multiple allergens,⁸ we further sought to determine whether the skin test profiles of a negative percutaneous MTII result with a corresponding positive intradermal test result (–P/+ID) correlated with positive nasal allergen challenge results evaluated by the acute development of allergic rhinoconjunctivitis (ARC) symptoms and by anterior rhinomanometry.

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Table 1. Allergen Concentrations for Serial Nasal Challenges

Allergen	Challenge 1	Challenge 2	Challenge 3	Challenge 4
House dust mite, AU/mL	10	100	1,000	1,000
Grasses, BAU/mL	212.5	2,125	21,250	21,250
Ragweed, AgE U/mL	0.1	1	10	10
Cat, BAU/mL	50	500	5,000	5,000
<i>Alternaria</i> , wt/vol	1:50,000	1:5,000	1:500	1:500

METHODS

Study Participants

This study was approved by the Saint Louis University institutional review board. We recruited 108 individuals aged 18 to 65 years with either symptoms of ARC or no symptoms at all. Participants were screened before skin testing using a questionnaire about symptoms of ARC and the likelihood of symptoms with exposure to mold, trees, grasses, weeds, cats, and house dust mite (HDM). Inquiries by investigators were made as necessary for verification. Eleven individuals were excluded from further study because of patient-identified exposure to dogs or cockroaches because skin tests for these allergens were not performed. Ninety-seven individuals were evaluated: 68 reported ARC to at least 1 of the aeroallergens being evaluated, and 29 reported no symptoms of ARC. Participants were then categorized by their skin test results, and 37 participants were further evaluated for their responses to 56 nasal challenges; among them were 12 participants with a positive ARC history and corresponding positive aeroallergen skin test results, 5 with a negative ARC history with negative skin test results, and 14 with 20 $-P/+ID$ profiles after initial skin testing. No participant who underwent nasal challenge reported a history of asthma, use of asthma medications, nasal polyps, or having received immunotherapy.

Allergen Extracts

Antigens for skin testing included 6 common local allergens: *Alternaria*, 1:20 wt/vol; mixed HDM (*Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*), 10,000 AU/mL; cat, 5,000 BAU/mL; mixed grasses (Kentucky, orchard, and timothy grass), 1:20 wt/vol (85,000 BAU/mL); mixed trees (oak, elm, sycamore, and maple), 1:20 wt/vol; and mixed ragweed (giant and short ragweed), 1:20 wt/vol (112 AgE U/mL). Allergen extracts for prick and MTII testing were glycerinated and were obtained from Greer Laboratories Inc (Lenoir, NC), except for cat (lyophilized and reconstituted using 0.4% phenol and saline), which was obtained from ALK-Abelló Inc (Round Rock, TX). Histamine, 1.8 mg/mL, was used as the positive control, and 50% glycerosaline was used as the negative control. For intradermal testing, extracts were diluted to 1:1,000 wt/vol for pollens and *Alternaria*, 5 BAU/mL for cat, 10 AU/mL for HDM, and 1,000-fold for the controls, from the same source lots (nonglycerinated, except for HDM and the negative control) as for the prick and MTII methods.

Skin Tests

Skin testing with the panel of 6 aeroallergens was performed on 97 participants using the skin prick and MTII methods. Antihistamines, tricyclics, and other medications that can cause false-negative skin test results were withheld for 72 hours before skin testing. Intradermal tests were applied only if the prick and MTII test results were negative. The prick method was performed as described by Pepys et al⁹ using lancets (ALK-Abelló Inc). The MTII was used according to the package insert. Intradermal tests were performed by superficial injection of 0.02 mL of the antigen solution using a 27-gauge needle to create a distinct and typical bleb. All skin tests were performed by the same individual. The wheal and erythema were recorded at 10 minutes for histamine controls and at 20 minutes for allergen extracts. A positive skin test result for the prick and intradermal methods was defined using the method described by Vanselow.¹⁰ A positive MTII result was defined per package insert. Participants with $-P/+ID$ profiles underwent repeated skin testing (within 6 months of initial testing) before nasal challenge. Intradermal test results that were negative on repeat were performed in triplicate to confirm the results.

Extract Concentrations Used for Nasal Challenges

The extract concentrations used for nasal challenge for each allergen are given in Table 1. Challenges included 3 stages of increasing concentrations and a fourth stage that repeated the concentration of the third stage. The concentrations were determined from pretrial studies, which elicited an allergic response in participants with ARC but without an irritant effect in nonrhinitic participants (data not shown). Aqueous solutions for nasal challenges were prepared from the same source lots as skin test extracts.

Nasal Challenges

Nasal challenges were performed out of season for seasonal allergens and after the resolution of upper respiratory tract infections. None of the participants reported the use of nasal sprays or oral corticosteroids. Antihistamines and decongestants were withheld for 72 hours before challenges. Participants with $-P/+ID$ profiles underwent single-masked nasal challenges to the corresponding aeroallergen. The positive control group consisted of 12 individuals from the ARC group with positive skin test reactions to the aeroallergen in question. The negative control group consisted of 5 individ-

uals from the group with a negative ARC history and negative skin test results. Metered-dose manual pumps (Schering, Kenilworth, NJ) delivered 2 sprays (0.1 mL per actuation) of the allergen solutions to each nostril at each challenge stage. The appropriate diluent control was given first, followed by sequential aeroallergen challenges administered every 15 minutes until participants either had positive challenge results or completed the 4 stages.

Anterior Rhinomanometry

Nasal allergen challenges were assessed by anterior rhinomanometry (MultiSpiro Inc, San Clemente, CA). Before each challenge session, the flow sensor was calibrated using a syringe, and the pressure was calibrated using a manometer. Resistance was calculated as pressure divided by flow. A reference pressure of $-1.5 \text{ cm H}_2\text{O}$ was used as a method of normalizing data between participants.

Calculation of Nasal Resistance and Nasal Resistance Response

Total nasal resistance (NR_T) was obtained by multiplying the intranasal resistance from each nostril and then dividing by their additive:

$$\text{NR}_T = \text{NR}_{\text{Right}} \times \text{NR}_{\text{Left}} / (\text{NR}_{\text{Right}} + \text{NR}_{\text{Left}})$$

This calculation eliminates error introduced by nasal cycling because NR_T remains effectively the same in the absence of unilateral anatomic disease.¹¹

The nasal resistance response ($\text{NR}_{\text{Response}}$) was determined by dividing the NR_T obtained after each serial challenge ($\text{NR}_{\text{Allergen}}$) by the NR_T obtained at baseline ($\text{NR}_{\text{Diluent}}$):

$$\text{NR}_{\text{Response}} = \text{NR}_{\text{Allergen}} / \text{NR}_{\text{Diluent}}$$

This calculation standardizes the different values obtained between different individuals or sessions.¹² A positive nasal challenge was defined as an $\text{NR}_{\text{Response}}$ 2.5-fold above baseline, determined from pretrial studies, and a symptom score of at least 4. The symptom scores, based on a scale from 0 to 12 validated by Lebel et al¹³ and used by Bousquet et al¹⁴ and Nelson et al,³ were corroborated by physical examination.

Statistical Analysis

The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and efficiency were calculated for each allergen based on each patient's history for skin prick and MTII tests. These 2 skin test methods were then compared with each other for each allergen according to the previous 5 measures using the χ^2 test or the Fisher exact test if at least 1 of the cell counts was less than 5. Comparisons between these 2 skin tests were also performed with all allergens combined using the Mantel-Haenszel test. We used analysis of variance to compare symptom scores and $\text{NR}_{\text{Response}}$ obtained from nasal challenges on $-P/+ID$ patients with those from positive and negative controls, separately.

RESULTS

Participant Characterization After Skin Testing

Of the 68 participants with a history of ARC, 3 were eliminated for dermatographism and 9 for negative skin test results with presumed perennial nonallergic rhinitis. Of the 29 participants without a history of atopic disease and reporting no ARC, 11 were eliminated for positive skin test results. The final study group included 56 individuals with a history of ARC and confirmed positive skin test results (14 of whom had 20 $-P/+ID$ tests), and 18 nonrhinitic individuals (16 with a negative history of ARC and negative skin test results and 2 with a negative history of ARC and $-P/+ID$ profiles). A total of 16 individuals with 22 $-P/+ID$ profiles were identified.

Participants With $-P/+ID$ Profiles

After repeated skin testing of 16 participants with 22 $-P/+ID$ tests, only 8 participants with 12 $-P/+ID$ profiles were confirmed. Two participants had positive MTII results for *Alternaria* that were previously negative. Six participants from the ARC group with a combined 8 $-P/+ID$ test results had negative intradermal test results on repeated testing. The 2 participants from the group without a history of ARC had confirmed $-P/+ID$ test results. There were no participants with a $-P/+ID$ profile to tree.

Comparison of Skin Prick and MTII Skin Tests With Patient History

The MTII method showed consistently higher sensitivities than the skin prick method for all aeroallergens tested (Table 2). The percentage of MTII tests that identified individuals reporting a probable history of ARC to an allergen ranged from 67.7% for *Alternaria* to 91.3% for cat, with an average of 77%. The prick test method had a sensitivity ranging from 32.3% for *Alternaria* to 82.6% for cat, with an average of 62%. Comparing the 2 methods for each allergen, the results showed that the sensitivity of MTII was significantly better only for *Alternaria* ($P = .006$). However, when combining all allergens together, MTII had a significantly higher sensitivity than the prick method ($P = .001$).

When participants were unsure of whether their symptoms were produced by exposure to a particular aeroallergen (ie, an equivocal history), results did not differ between the prick and MTII methods. Of the 56 participants with a probable history of ARC and positive skin test reactions to the corresponding aeroallergen, 19 reported equivocal histories to other aeroallergens in 29 cases. In 28 cases, participants had the same results for the prick and MTII methods (17 positive and 11 negative skin test results), with only 1 participant having a negative prick test reaction to grass with a positive MTII result.

Comparing MTII and prick testing for specificity, there was no significant difference found for any allergen or for all allergens combined ($P = .13$), although the prick tests showed higher specificities for most aeroallergens tested than the MTII method (Table 2). The average specificity for the

Table 2. Sensitivities, Specificities, Predictive Values, and Efficiencies for Each Aeroallergen for the Multi-Test II and Skin Prick Test Methods*

Allergen	Sensitivity, No. (%)	Specificity, No. (%)	PPV, No. (%)	NPV, No. (%)	Efficiency, No. (%)
Skin prick test					
<i>Alternaria</i>	10/31 (32.3)	36/40 (90.0)	10/14 (71.4)	36/57 (63.2)	46/71 (64.8)
HDM	18/37 (48.6)	32/34 (94.1)	18/20 (90.0)	32/51 (62.7)	50/71 (70.4)
Cat	19/23 (82.6)	41/47 (87.2)	19/25 (76.0)	41/45 (91.1)	60/70 (85.7)
Tree	24/38 (63.2)	29/32 (90.6)	24/27 (88.9)	29/43 (67.4)	53/70 (75.7)
Grass	15/22 (68.2)	33/40 (82.5)	15/22 (68.2)	33/40 (82.5)	48/62 (77.4)
Ragweed	29/38 (76.3)	29/33 (87.9)	29/33 (87.9)	29/38 (76.3)	58/71 (81.7)
Average	62%	89%	80%	74%	76%
Multi-Test II					
<i>Alternaria</i>	21/31 (67.7)	33/40 (82.5)	21/28 (75.0)	33/43 (76.7)	54/71 (76.1)
HDM	26/37 (70.3)	31/34 (91.2)	26/29 (89.7)	31/42 (73.8)	57/71 (80.3)
Cat	21/23 (91.3)	36/47 (76.6)	21/32 (65.6)	36/38 (94.7)	57/70 (81.4)
Tree	28/38 (73.7)	29/32 (90.6)	28/31 (90.3)	29/39 (74.4)	57/70 (81.4)
Grass	16/22 (72.7)	32/40 (80.0)	16/24 (66.7)	32/38 (84.2)	48/62 (77.4)
Ragweed	32/38 (84.2)	28/33 (84.8)	32/37 (86.5)	28/34 (82.4)	60/71 (84.5)
Average	77%	84%	79%	81%	80%

Abbreviations: HDM, house dust mite; NPV, negative predictive value; PPV, positive predictive value.

*Sensitivities and NPVs were significantly higher for Multi-Test II ($P = .001$ and $.04$, respectively) than for the prick method when all allergens were combined. Specificities, PPVs, and efficiency were not significantly different between the Multi-Test II and skin prick tests ($P = .13$, $.69$, and $.13$, respectively).

prick test was 89%, ranging from 82.5% for grass to 94.1% for HDM. The average specificity for the 6 allergens tested using the MTII method was 84%, ranging from 76.6% for cat to 91.2% for HDM.

The average PPV was 79% for MTII (range, 65.6% for cat to 90.3% for trees) and 80% for the prick test (range, 68.2% for grass to 90.0% for HDM); the average NPV was 81% for MTII (range, 73.8% for HDM to 94.7% for cat) and 74% for the prick test (range, 62.7% for HDM to 91.1% for cat); and the average efficiency was 80% for MTII (range, 76.1% for *Alternaria* to 84.5% for ragweed) and 76% for the prick test (range, 64.8% for *Alternaria* to 85.7% for cat) (Table 2). These 2 methods did not show any significant difference for any allergen comparing PPV, NPV, or efficiency. However, when all allergens were combined, the MTII method showed a significantly higher NPV than the prick method ($P = .04$).

Results of Intradermal Skin Tests and Nasal Challenges

The intradermal tests, because they were performed only when the prick and MTII test results were negative for a given aeroallergen, were not directly comparable and so were considered separately. The sensitivity of the intradermal method was, on average, 17% for the combined aeroallergens, ranging from 0% for cat and tree to 36.4% for HDM (Table 3).

All 8 participants with 12 confirmed $-P/+ID$ profiles and 6 participants with 8 intradermal test results that were negative on repeated testing completed the 4 stages of sequential nasal challenges to the relevant aeroallergen without notable response (Figure 1). The ranges of $NR_{Response}$ were 0.47 to 1.55 for the $-P/+ID$ group and 0.69 to 1.86 for the negative control group (Table 4). The responses of these 2 groups were

Table 3. Sensitivity of Intradermal Skin Tests for Each Aeroallergen*

Allergen	Sensitivity, No. (%)
<i>Alternaria</i>	1/10 (10.0)
House dust mite	4/11 (36.4)
Cat	0/2
Tree	0/11
Grass	2/6 (33.3)
Ragweed	1/6 (16.7)
Average	17%

*Sensitivities were determined by the number of positive intradermal skin test results in patients with a probable history not identified by the skin prick and Multi-Test II methods.

not significantly different ($P = .18$). In contrast, the $NR_{Responses}$ for the positive control group ranged from 2.86 to 13.35, which was significantly different from those for the $-P/+ID$ group ($P < .001$). These results were corroborated by the symptom scores, which ranged from 4 to 11 for the positive control group and from 0 to 1 for the negative control group. The $-P/+ID$ group had symptom scores that were similar to those of the negative control group ($P = .26$), with a maximal score of 3, and significantly different from those of the positive control group ($P < .001$).

DISCUSSION

Based on patient histories, these results demonstrate that MTII has a higher sensitivity and NPV than the skin prick method when all allergens are combined. This study further demonstrates the low correspondence of intradermal skin tests to patient history. As evaluated by nasal challenge, none of the positive intradermal test results, with corresponding

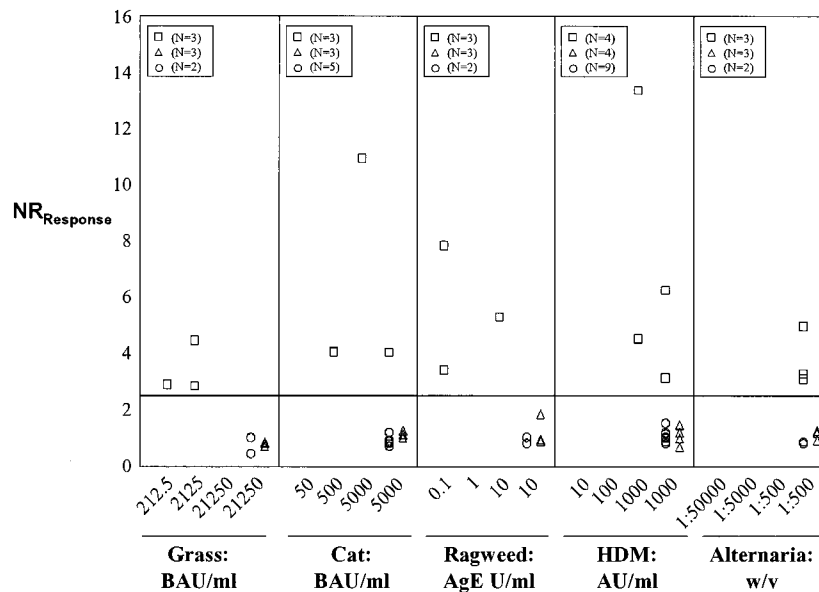


Figure 1. Nasal resistance response ($NR_{Response}$) in individuals with negative Multi-Test and positive intradermal test profiles ($\circ$), the positive control group ($\square$), and the negative control group ($\triangle$). HDM indicates house dust mite.

Table 4. Nasal Resistance Responses ($NR_{Responses}$) and Symptom Scores From Nasal Challenges for Each Group

Group	Challenges, No.	Symptom scores, range (mean $\pm$ SD)*	$NR_{Response}$ range (mean $\pm$ SD)†
Positive controls	16	4–11 (7.31 $\pm$ 2.06)	2.86–13.35 (5.28 $\pm$ 3.02)
Negative controls	16	0–1 (0.06 $\pm$ 0.25)	0.69–1.86 (1.09 $\pm$ 0.3)
–P/+ID	20	0–3 (0.3 $\pm$ 0.8)	0.47–1.55 (0.97 $\pm$ 0.22)

Abbreviation: –P/+ID, negative percutaneous Multi-Test II skin test results with positive intradermal skin test results.

*Symptom scores for the –P/+ID and the negative control groups were significantly different from those for the positive control group ($P < .001$) but were not significant compared with each other ($P = .26$).

†The $NR_{Responses}$ for the –P/+ID and the negative control groups were significantly different from those for the positive control group ($P < .001$) but were not significant compared with each other ($P = .18$).

negative MTII results, identified ARC. In addition, intradermal skin tests had poor reproducibility. This study adds to the mounting evidence that brings into question the value of routinely performing intradermal testing when epicutaneous and percutaneous skin test results are negative.

We found that MTII had 77% sensitivity and an 81% NPV in identifying clinically important respiratory allergens as evaluated by history of ARC, which were higher than the values using the skin prick method (62% sensitivity and a 74% NPV). Intradermal tests were considered separately to determine their value when the skin prick and MTII methods

had negative results, and they corresponded to patient history only 17% of the time, with 59% of positive intradermal test results occurring in individuals without a history of ARC to the allergen in question. This study adds to previous studies^{7,15,16} that have examined the accuracy and efficiency of the percutaneous skin test method compared with other skin test methods.

Because patient history can be flawed, we performed nasal challenges to objectively determine patient sensitivity to the allergen in question. We found no positive nasal challenges in individuals with –P/+ID profiles. The patients' symptom scores, physical examination findings, and intranasal resistances were well within the range of the negative control group and significantly different from the positive control group. In contrast, positive nasal challenge results were seen in participants with positive percutaneous test results and a history of ARC. There is no true gold standard for confirming nasal allergy. It has been argued that nasal challenges may be superphysiologic, causing some investigators to supplement nasal challenges with seasonal symptoms/pollen counts, whereas natural exposures (eg, park studies or cat apartment challenges) are physiologic.¹⁷ Nonetheless, studies^{3,9,13,18–21} have shown a strong correlation of the presence of respiratory allergy to nasal challenges. Therefore, despite the acknowledged limitations of our study design, our results suggest that a positive intradermal skin test result does not indicate the presence of allergic disease and that in the presence of a negative MTII skin test result, a follow-up intradermal skin test would be of little additional value.

In this study, intradermal reproducibility was low. Generally, the literature has demonstrated that intradermal testing is more reproducible than the prick method, and it is for this

reason that Turkeltaub²² used the erythema produced by intradermal testing as the basis for biological standardization of allergenic extracts. Gottlieb et al,²³ however, found poor reproducibility of intradermal tests when performed 4.2 to 11.4 months after initial testing. In our study, there were intervals of up to 6 months between repeated testing, and this may account for the poor reproducibility of intradermal tests observed.

In this study, we found 2 -P/+ID profiles to *Alternaria* with positive MTII test results on repeated testing. Because these participants reported a probable history of ARC to *Alternaria*, this may suggest that for weaker antigens, such as mold, intradermal testing may be helpful in identifying clinically relevant sensitivity when the MTII result is negative. However, in this study, we also found -P/+ID profiles to *Alternaria* without a history of ARC that had negative nasal challenges, emphasizing the importance of clinical correlation. Indeed, a recent study by Bobbitt et al²⁴ reports that "[i]ntracutaneous testing (1:1,000 dilution) did not discriminate between atopic and nonatopic phenotypes," stating that intradermal tests for molds at a 1:1,000 dilution could lead to irritant reactions, making it difficult to differentiate between irritant and immune-mediated responses. Thus, particular caution should be taken in interpreting a positive intradermal test result to mold.

Several possibilities have been offered to explain the high number of false-positive results that are observed with intradermal skin testing. The most often suggested mechanism is that of an irritant effect due to a nonspecific inflammatory reaction.^{10,25,26} Glycerin, used in extracts for allergen stability, has been implicated as a possible irritant in the past^{10,27,28} and is the reason that predominately aqueous extracts are used for the performance of intradermal tests. Although some glycerin was present in the final HDM extract (0.05% glycerin) used for intradermal testing in the present study, we found no positive reactions to the intradermal negative control of glycerosaline at the same concentration. The high number of false-positive intradermal test results found using the glycerin-free cat extract suggests that components in extracts other than excipients may be capable of causing local responses via irritant or other non-IgE-mediated mechanisms. It has been suggested that lysine-sugar groups in some allergens may cause such local responses.²⁹ The number of lysine-sugar groups per molecule is maximal in house dust allergen and minimal in pollen, corresponding to our finding of more false-positive intradermal reactions to HDM and fewer to pollens.

Although false-positive intradermal test reactions to aeroallergens might actually detect low levels of specific IgE (albeit without clinical significance), there is evidence against this being a generally applicable explanation. Brown et al⁵ found that there is no clear difference in intradermal reactivity for allergic and nonallergic patients to individual allergens and that when all epicutaneous test results are negative, more nonallergic patients react to subsequent intradermal testing. In the present study, not only did we have many positive

intradermal skin test results in individuals reporting an unlikely history to the aeroallergen in question, but we also found 2 nonatopic individuals with completely negative histories of ARC and negative skin prick and MTII skin test results that had positive intradermal skin test results, 1 to HDM and 1 to cat.

There has been mounting evidence that intradermal tests performed at concentrations of 1:1,000 wt/vol (50 times more dilute than the 1:20 wt/vol extracts commonly used for prick and MTII tests) do not correlate with either respiratory allergy or the presence of IgE.⁴ Brown et al⁵ found that when allergen concentrations for intradermal testing were only 50 times weaker than for prick testing, intradermal test results correlated poorly with clinical allergy and serum IgE levels. Although Indrajana et al³⁰ reported that the antigen threshold for producing a positive intradermal reaction is 250 times less than that for producing a positive prick test result, Stenius et al²⁰ found that the intradermal threshold concentration may be as much as 1,000 times less, suggesting that even more dilute aeroallergen concentrations than 1:1,000 wt/vol might detect IgE reactivity using intradermal testing. It is possible that with decreasing extract concentrations, and thereby extract components that have a nonspecific irritant effect, intradermal testing may correlate better with IgE level and clinical status. In agreement with this, Perera et al³¹ found that correlation was improved with decreasing concentrations of allergen, but they still found only 55% agreement between intradermal test results and radioallergosorbent test results at concentrations of 10⁻⁸ g/mL.

Although it is clear that intradermal skin test reactions to aeroallergens produce many false-positive skin test results, the mechanism is still unclear and needs further elucidation. Because of the different routes of sensitization, exposure, and the chemical nature of drugs, insect venoms, and other biologicals, our study results may not be applicable to intradermal testing with these agents. Furthermore, because our study population was aged 18 to 65 years, the results of this study may not reflect the potential sensitivity, specificity, or predictive values of aeroallergen skin tests in the very young or very old.

Under the conditions of this study, there is a high correspondence of the skin prick and MTII test methods to patient history. However, the MTII skin test method has a significantly higher sensitivity than the skin prick method compared with patient history without compromising specificity. When skin prick and MTII skin test results are negative, the presence of a positive intradermal skin test result is unlikely to identify clinically important respiratory allergy. Further studies are required to define particular clinical scenarios in which intradermal tests may have a useful role in identifying aeroallergen sensitivity (eg, confirming borderline test results and assessing sensitivity to weaker allergens).

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